

AMENDMENTS TO THE SPECIFICATION

Please replace the paragraph beginning at page 14, lines 15-26, with the following amended paragraph:

T-bet is unique in that it is the only T-box protein to be tyrosine phosphorylated. There are two consensus tyrosine phosphorylation sites at aa 328-336 and 526-534 of human T-bet and 327-335 and 521-529 of murine T-bet. A nuclear localization sequence is also present at amino acids 498-501 of human T-bet and 493-496 of murine T-bet. Mapping experiments locate two transactivation domains, one 5' and one 3' of the T-box domain. The data shown herein demonstrate that T-bet binds to a consensus T-box site (defined by target site selection in vitro as 5'-GGGAATTTACACCTAGGTGTGAAATTCCC-3') (SEQ ID NO:5) and to a T-box site in the IL-2 promoter. T-bet is expressed only in the thymus and in the peripheral lymphoid system. In the periphery, T-bet is expressed only in Th1 cells where it is induced both in response to TcR stimulation and to IL-12. In the thymus levels of T-bet are highest in DN and Rag2-/- thymocytes.

Please replace the paragraph beginning at page 72, line 28, through page 73, lines 1-7, with the following amended paragraph:

The T-box domain has recently been co-crystallized with DNA and demonstrates a novel sequence-specific DNA recognition architecture in which the protein contacts DNA in both the major and minor grooves (Müller, C.W. and Herrmann, B.G. 1997. *Nature* 389, 884-888). The consensus T box binding site as defined by target site selection in vitro is a palindrome 5'-GGGAATTTACACCTAGGTGTGAAATTCCC-3' (SEQ ID NO:5). Inspection of the IL-2 promoter reveals an excellent T-box site at -240 to -220 just 5' of the NFκB site to which recombinant T-bet protein binds. The binding of T-bet to the IL-2 promoter explains its isolation in the yeast one hybrid screen where the readout depended simply on binding of T-bet to the T box site in the IL-2 promoter to drive an artificial reporter. Despite the clear repression of IL-2 promoter activity by T-bet, a decrease in IL-2 promoter activity upon mutation of the T-box site has been observed. However, that T-bet can still repress the transactivation of an IL-2 promoter construct in which that T-box site has been mutated. This suggests either the presence

of another T-box site in the IL-2 promoter, or interference with another positively acting factor that binds close by. A good candidate for this factor is an activity described by Rothenberg and colleagues that binds to a site TGGGCC just adjacent to the T-box site (Chen, D. and Rothenberg, E.V. 1994. *J. Exp. Med.* 179, 931-942).